REMARKS

Claims 1-3, 5-9, 26 and 27 remain pending in the application. Claims 11-25 were withdrawn from consideration. Claims 1-3, 5-9, 26 and 27 stand finally rejected. No claims were allowed.

Applicants would also like to point out that their claim of foreign priority under 35 U.S.C § 119 has not been acknowledged. Applicants note that a certified copy India Patent Application No. 156/MAS/2003 was submitted to the Office on August 22, 2005, thereby completing the requirements for a claim of foreign priority under § 119. Applicants respectfully request that their claim of foreign priority of 156/MAS/2003 be acknowledged in the next official communication.

Claims 1 and 6-9 have been amended, as requested by the Examiner, to replace the officially adopted name "rabeprazole" with an IUPAC name for the compound. Support for the amendments can be found throughout the specification as originally filed, *e.g.*, page 1, lines 8-9. No new matter has been introduced by these amendments.

Claims 11-25 have been cancelled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications directed to the canceled subject matter and/or any other subject matter disclosed in the instant specification.

Reconsideration and allowance of the finally rejected claims in view of the amendments above and the remarks below are respectfully requested.

Claim Rejections – 35 U.S.C. § 102

Claims 1-3, 5-9, 26 and 27 were rejected under 35 U.S.C. §§ 102(a), (b) and/or (e) as allegedly anticipated by Takashi et al. (JP 2001-39975) (hereinafter "Takashi"), Souda et al. (US 5,045,552) (hereinafter "Souda") and Reddy et al. (WO 03/082858) (hereinafter "Reddy") for the reasons set forth in the previous Office Action. According to the Examiner, Takashi, Souda and Reddy specifically

disclose the instant rabeprazole sodium salt. The term "Form Z," according to the Examiner, does not offer any demarcation of the claimed product from the prior art crystalline product. Applicants respectfully traverse this basis for rejection.

Contrary to the Examiner's contention, Takashi, Souda and Reddy do not specifically disclose the instant rabeprazole sodium salt. Claims 1-3, 5-9, 26 and 27 are directed to crystalline Form Z of rabeprazole sodium having substantially the same X-ray diffraction pattern as shown in Figure 1. Applicants submit that by incorporating the X-ray diffraction pattern as shown in Figure 1, the claims adequately distinguish the instant crystalline rabeprazole sodium form from the material disclosed in Takashi, Souda and Reddy. *See Ex parte Havens*, 2003 WL 21279863 (BPAI 2003) ("The examiner has provided no evidence or scientific reasoning to show that the delavirdine mesylate disclosed and claimed [in the prior art reference] is in the [claimed] crystal form. Therefore, the examiner has not made out a *prima facie* case of anticipation by inherency.").

Souda describes in Example 33 a process for preparing rabeprazole sodium salt. No X-ray diffraction data is presented. There is no teaching, or even a suggestion, in Souda of crystalline rabeprazole sodium polymorphs, let alone the particular crystalline Form Z disclosed and claimed in the instant application. Takashi appears to describe a crystal of a rabeprazole salt:acetone complex having an X-ray diffraction pattern at page 5 substantially different from that shown in Figure 1 of the instant specification. Reddy discloses rabeprazole sodium forms X and Y, also having X-ray diffraction patterns substantially different from that shown in Figure 1 of the instant specification. Because the instantly claimed rabeprazole sodium Form Z and the rabeprazole sodium forms disclosed in the cited prior art are distinct molecular structures (as evidenced by their different X-ray diffraction patterns, when given), Applicants submit that claims 1-3, 5-9, 26 and 27 are not anticipated under §§ 102(a), (b) and/or (e), and reconsideration of this basis for rejection is respectfully requested.

The Examiner at page 3 of the Office Action states that "in the strictest sense, polymorphs are different crystalline forms of the **same pure substance** in

which the molecules have different arrangements and/or different confirmations of the molecules." In doing so, the Examiner appears to be taking the position that new polymorphs are unpatentable *per se* over the originally identified compound or previously identified polymorphs of the same compound. But this is surely not the law. The Federal Circuit and the CCPA have consistently found new polymorphs to be patentable over other forms of the same compound (including other polymorphs), thereby fulfilling the novelty requirement. *See, e.g.*, *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043 (Fed. Cir. 1995) (ranitidine form 2 novel over form 1); *Bristol-Myers Co. v. U.S. Int'l Trade Comm'n*, 892 F.2d 1050, 1989 WL 147230 (Fed. Cir. Dec. 8, 1989) (unpublished decision) (Bouzard cefadroxil monohydrate novel and unobvious over other cefadroxil forms); *Silvestri v. Grant*, 496 F.2d 593 (CCPA 1974) (ampicillin B patentably distinct from ampicillin A); *In re Irani*, 427 F.2d 806 (CCPA 1970) (crystalline anhydrous ATMP novel and unobvious over amorphous ATMP); *In re Cofer*, 354 F.2d 664 (CCPA 1966) (crystalline 2,2-B novel and unobvious over liquid 2,2-B). Indeed, the Examiner recognizes the novelty of the rabeprazole sodium X and Y forms claimed in the instant application at page 9 of the Office Action:

> The nature of the invention is the preparation of novel crystalline forms Z of rabeprazole sodium and compositions. (Emphasis added.)

Because the prior art fails to disclose the specific solid state characteristics for rabeprazole sodium Form Z claimed in instant application, Applicants submit that claims 1-3, 5-9, 26 and 27 are not anticipated under §§ 102(a), (b) and/or (e), and reconsideration of this basis for rejection is respectfully requested.

Claim Rejections – 35 U.S.C. § 103

Claims 1-3, 5-9, 26 and 27 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over the combined teachings of Takashi, Souda and Reddy in view of Halbein et al., Brittain et al., Muzaffar et al., Jain et al.,

Chemical & Engineering News, U.S. Pharmacopia, and the Concise Encyclopedia of Chemistry for the reasons set forth in the previous Office Action. According to the Examiner, Takashi, Souda and Reddy teach the crystalline form of rabeprazole and rabeprazole sodium, as well as pharmaceutical compositions. Further, according to the Examiner, Halbein et al., Muzaffar et al. and Jain et al. teach that compounds can exist in different crystalline forms, and Chemical & Engineering News, U.S. Pharmacopia and the Concise Encyclopedia of Chemistry teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Thus, according to the Examiner, it would appear obvious to one skilled in the art that the instant compound would exist in different polymorphic forms. Applicants respectfully traverse this basis for rejection.

First, as discussed above with respect to the § 102 rejection, there is no teaching, or even a suggestion, in Takashi, Souda or Reddy that rabeprazole sodium can exist in other polymorphic forms, let alone the particular Form Z of the instant application. This alone is enough to overcome the Examiner's obviousness rejection. *See Ex parte Havens*, *supra* ("The examiner's obviousness rejection seems to suffer the same infirmity as her anticipation rejection . . . The examiner has provided no evidence or convincing reason why the prior art disclosure of delavirdine mesylate in an undefined state would have suggested the specific S and T crystal forms that are the subject of the instant claims.") (emphasis added). The ancillary references cited by the Examiner merely provide general background information relating to the study and preparation of polymorphs or case histories of specific polymorphic compounds (none of which are rabeprazole sodium), and thus add nothing over the primary references.

Contrary to the Examiner's position, the proper test for obviousness in this case is not whether the existence of rabeprazole sodium polymorphs is suggested by the prior art, but whether it would have been obvious to make the particular rabeprazole sodium Form Z claimed in the instant application based on the prior art:

> The law of § 103 requires quite a different inquiry from that conducted by the ALJ. The correct inquiry is not whether the Bouzard monohydrate [polymorph] could have been produced by manipulation of other cefadroxil processes, once the existence of the Bouzard monohydrate was known. The question is whether it would have been obvious to make the Bouzard monohydrate, based on the prior art.

Bristol-Myers Co. v. U.S. Int'l Trade Comm'n, *supra* (emphasis added).

Here, the references cited by the Examiner suggest at most the possibility of rabeprazole sodium polymorphs. The Examiner has pointed to nothing in the cited references, however, that would suggest to one skilled in the art the particular rabeprazole sodium Form Z of the instant application, or a method for its preparation.

The Examiner at p. 5 of the Office Action states:

> As clearly stated by one having ordinary skill in the art in Brittain . . . , as well as set forth by the court in In re Cofer (CCPA 1966) 354 F2d 664, 148 USPQ 268, Ex parte Hartop 139 USPQ 525, that a product which is merely a different form of a known compound, not withstanding that some desirable results are obtained therefrom, is unpatentable. The instant claims are drawn to the ***same pure substance*** as the prior art that only have different arrangements and/or different conformations of the molecule. A mere difference in a physical property is a well known conventional variation for the same pure substance is *prima facie* obvious.

As with the § 102 rejection, the Examiner again appears to be taking the position that new polymorphs unpatentable *per se*. But as stated by the Board of Patent Appeals & Interferences in a recent polymorph decision:

> The use of per se rules flouts § 103 and the fundamental case law applying it. . . . [R]eliance on per se rules of obviousness is legally incorrect and must cease.

Ex parte Andrews, Appeal No. 2002-0941 (BPAI 2003, relating to 09/166,445, now US 6,713,481 B1) (quoting *In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995)). As

discussed above, courts have consistently found new polymorphs to be patentable where the prior art failed to suggest the particular form claimed.

The Examiner's reliance on *In re Cofer* and *Ex parte Hartop* is misplaced in this case. *Cofer* actually held the claimed crystalline 2,2-bis patentable because

> [T]he board failed to address . . . whether the prior art suggests the particular structure or form of the compound or composition as well as suitable methods of obtaining the structure or form. (Emphasis added.)

Here, as in *Cofer*, the references cited by the Examiner neither disclose nor suggest the particular rabeprazole sodium Form Z of the instant application, nor a method for preparing them.

The Board of Patent Appeals & Interferences has recently cautioned against the reliance on *Ex parte Hartop* in polymorph applications. As stated in *Ex parte Gala*:

> The examiner relies heavily on this proposition of law set forth in *Ex parte Hartop* . . : "[m]erely changing the form, purity or another characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable." According to the examiner, polymorph form 2 loratadine is merely another form of an old product (polymorph form 1 loratadine) and both forms possess the same utility. Accordingly, the examiner concludes that applicants' claims, reciting polymorph form 2 loratadine, are unpatentable. We disagree. Here, we invite attention to *In re Cofer* . . . , where the court substantially discredited PTO reliance on the above-quoted proposition of law in *Hartop*. Like the situation presented in *Cofer*, the examiner in this case has not adequately established that the prior art (1) suggests the polymorph form 2 of loratadine; or (2) discloses or renders obvious a method for making the polymorph form 2 of loratadine. (Emphasis added.)

Appeal No. 2001-0987 (BPAI 2001, relating to Application No. 09/169,109, now US 6,335,347 B1); *see also Ex parte Andrews*, *supra* ("[T]he principal of law

enunciated in *Ex parte Hartop* . . . has been substantially discredited in *In re Cofer* . . .").

Because the prior art neither discloses nor suggests the particular rabeprazole sodium Form Z of the instant application, Applicants submit that claims 1-3, 5-9, 26 and 27 are not *prima facie* obvious under § 103(a), and reconsideration of this basis for rejection is respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 1-3, 5-9, 26 and 27 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description and/or enablement requirements. According to the Examiner, there is a lack of description as to whether the compositions are able to maintain the compounds in the crystalline forms claimed (such as when they are in solution), and the specification lacks direction or guidance for maintaining the compounds in the crystalline forms claimed. Applicants respectfully traverse this basis for rejection.

According to MPEP § 2163:

> An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966. (Emphasis added.)

Similarly, according to MPEP § 2164.08:

> All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject matter is encompassed by the claims. (Emphasis added.)

The subject matter of claims 1-3, 5-9, 26 and 27 is directed to crystalline Form Z of rabeprazole sodium having substantially the same X-ray diffraction pattern as shown in Figure 1, as well as compositions comprising the same. Contrary to the Examiner's positions, the claims contain no limitation requiring

that Form Z be maintained indefinitely, or that it be the only form present in the compositions. Applicants submit that Examples 1-3 of the instant specification clearly describe and enable the preparation of rabeprazole sodium Form Z and compositions comprising the same.

Applicants further submit that reading the claims to encompass compounds and compositions where all crystalline structure of rabeprazole sodium Form Z is lost (and hence its solid state characteristics are also lost) is contrary to the plain meaning of the claim language. Claims 1-3, 5-9, 26 and 27 specifically recite "crystalline Form Z of rabeprazole sodium, having substantially the same X-ray diffraction pattern as shown in Figure 1," meaning that rabeprazole sodium in solution (and thus lacking any crystalline structure with the specifically recited XRPD) is outside the scope of these claims. Because the specification describes and enables the full scope of the claimed subject matter, claims 1-3, 5-9, 26 and 27 are not invalid under § 112, first paragraph, and reconsideration of this basis for rejection is respectfully requested.

Claims 1 and 6-9 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. According to the Examiner, "Form Z" is not a universal identification of compounds and "rabeprazole" is a trademark/trade name. Applicants respectfully traverse this basis for rejection.

Regarding the term "Form Z," claims 1 and 6-9 specifically recite "having substantially the same X-ray diffraction pattern as shown in Figure 1," which Applicants submit adequately defines the metes and bounds of the claimed subject matter. Reconsideration of this basis for rejection is respectfully requested.

Regarding the term "rabeprazole," as explained in Applicant's prior Amendment and Response, rabeprazole is not a trademark or tradename, but rather the USAN name accepted by the FDA as the official name for 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H-benzimidazole. As such, the term is not indefinite. However, solely in the interest of expediting prosecution, claims 1 and 6-9 have been amended to replace "rabeprazole" with

"2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H-benzimidazole." Reconsideration of this basis for rejection is respectfully requested.

Double Patenting

Claims 1-3, 5-9, 26 and 27 were provisionally rejected under the judicially created doctrine of obviousness-type patenting as allegedly obvious over claims 1-3, 5-9, 11-13, 26 and 27 of copending U.S. Patent Application No. 10/786,556 (since the instant application is Application No. 10/786,556, applicants will assume the Examiner intended Application No. 10/505,826) in view of Halbein et al., Muzaffar et al., Jain et al., Chemical & Engineering News, U.S. Pharmacopia, and the Concise Encyclopedia of Chemistry for the reasons set forth in the previous Office Action.

Applicants submit that it is inappropriate at this time to address the double patenting rejection because it is only a provisional application. The claims involved have not been allowed and are still subject to amendment. Applicants will address the double patenting rejection upon indication that one or more of the claims involved are allowable. Applicants would like to point out at this time, however, that the claims of each application as presently written are allowable over the other for the reasons given above in response to the § 103 rejection.

CONCLUSION

It is now believed that claims 1-3, 5-9, 26 and 27 are now in condition for allowance, early notice of which would be appreciated. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number indicated below to discuss the same. No fees are believed due at this time. If, however, any fees are due, the Commissioner is authorized to charge such fees

to our Deposit Account No. 50-3221 in the name of Dr. Reddy's Laboratories, Inc..

Respectfully submitted,

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